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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,939	03/31/2004	Jimo Borjigin	056100-5035-US	4917
9629 7590 01/05/2009 MORGAN LEWIS & BOCKIUS LLP 1111 PENNSYLVANIA AVENUE NW WASHINGTON, DC 20004				
EXAMINER EBRAHIM, NABILA G				
ART UNIT 1618		PAPER NUMBER		
MAIL DATE 01/05/2009		DELIVERY MODE PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/812,939

**Applicant(s)**

BORJIGIN, JIMO

**Examiner**

Nabila G. Ebrahim

**Art Unit**

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**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 March 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-11, 15-19 and 24-26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11, 15-19 and 24-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/S508)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date \_\_\_\_\_

### DETAILED ACTION

Receipt of claims' amendments and applicant's arguments dated 3/4/2008 is acknowledged.

#### ***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-11 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant while recites an agent that modulates a preselected biological condition controlled by the circadian clock. The specification defines the agent as follows: "the term agent refers to any compound which is pharmacologically active and/or modulates a biological condition in a subject". The specification does not describe the "agent" sufficiently, there are no examples of this "agent", no structure, and no mode of action that conveys a sense that Applicant had possession of the claimed invention. There is no structure/function relationship to show that applicant envisioned the genus of such an agent defined by function only at the time of filing. There is no reasonable number of species defined showing a structure/function relationship to support the definition by function only, and the term is not a term of art in which one would readily envision the genus described by function only.
3. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim recites "the physiological state of a tissue". The specification does not support this recitation. Applicant claims that the phrase is supported in paragraph 37 of the instant specification. However, the said paragraph supports "biological condition". There are many differences between biological conditions and physiological state of a tissue for example "biological conditions" demonstrates the status of the living tissue at a moment of the organism's life. The "physiological state of a tissue" is related to the functions which this tissue and other tissues exert to keep the said tissue alive. The meaning is different. In accordance with MPEP 714.02 applicants should specifically point out support for the generic concept of claim 8 using the expression "the physiological state of a tissue"

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites, "wherein the preselected biological condition is the physiological state of a tissue", the phrase "physiological state" is not clear since all tissues are in a specific physiological state at all times. The claim is vague.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 1-11,15-19 and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over ***W. J. Drijfhout et al.*** Exogenous melatonin entrains rhythm and reduces amplitude of endogenous melatonin: An in vivo microdialysis study, Journal of Pineal Research Volume 20 Issue 1 Page 24-32, January 1996 (Drijfhout) in view of ***Josephine Arendt***, Melatonin and the pineal gland: influence on mammalian seasonal and circadian physiology, *Reviews of*

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*Reproduction* (1998) 3, 13–22 (Josephine) and further in view of **Xing SUN et al.** Circadian 5-HT production regulated by adrenergic signaling. *PNAS*. 2 April 2002, Vol. 99, No. 7, pages 4689–4691, see pages 1–15 (Sun) and further in view of Lu et al. "Pineal regulation of circadian rhythms of 2-deoxy[<sup>14</sup>C] glucose uptake and 2[<sup>125</sup>I]iodomelatonin binding in the visual system of the house sparrow, *Passer domesticus*" *J Comp Physiol A*(12993) 173:765–774 (Lu) and Further in view of Ziyal et al., Combined supra/infatentorial-transsinus approach to large pineal region tumors, *J Neurosurg* 88: 1050–1057, 1998 (Ziyal).

Krijfhout teaches that the circadian rhythm of melatonin production was studied using on-line, in vivo microdialysis in the rat pineal gland. With this technique it was possible to record a pronounced melatonin rhythm with very high time resolution. Three phase-markers of the rhythm were calculated from the data, indicating increase (IT<sub>50</sub>), decrease (DT<sub>50</sub>) and amplitude of the rhythm. Comparing these phase markers led to several conclusions. The data presented provide us with new information about the nature of entrainment by melatonin. Since the present development of melatonergic agents for clinical use focuses on the entrainment capacity, effects of these compounds on amplitude of circadian rhythms needs to be addressed. In vivo microdialysis seems to be a good technique for that (abstract). The study also discloses that the agents such as melatonin have an effect of sleep disorders (page 24). Regarding the surgery steps recited in claims 15–19, the reference teaches using a drill

One hole was drilled on each side of the temporal bone, inserting the probe of the monitoring device.

**Briefly the reference teaches that the circadian rhythm (clock) that produces melatonin was known and that the rhythm could be modulated by contacting the pineal by agents such as melatonin itself. The rhythm could be monitored by microdialysis as a good technique for the monitoring.**

The study does not disclose the treatment of condition or disorders other than sleep disorders.

Josephine teaches that exogenous melatonin can entrain, circadian rhythms in rodents and humans. It can lower body temperature and induce transient sleepiness. These properties indicate that melatonin can be used therapeutically in circadian rhythm disorder. The reference also teaches that Successful outcomes have been reported, for example in jet lag and shift work, and with cyclic sleep disorder (abstract), insomnia, some problems of old age, and some psychiatric disorders (page 20).

**The reference teaches the melatonin can be used as therapeutic agent for some conditions such as psychiatric problems and sleeping disorders.**

Note that the steps recited in instant claim 1 which are: 1) monitoring an organ, 2) contacting the organ with an agent and 3) monitoring again to find out the effect are previously known in the art for detecting the effect of a drug and/or diagnosis of diseases such as the chemical stress test done for diagnosis of cardiovascular conditions.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use melatonin and/or its agonists to treat conditions such as sleeping disorders, behavioral problems and monitor its effect according to the method disclosed by Drijfhout.

Though the step of lifting the tissue over the pineal tissues is an expected step, it is noted that Drijfhout did not literally disclose this step.

Sun teaches using on-line microdialysis, to monitor *in vivo* dynamics of pineal 5-hydroxytryptamine (5-HT; serotonin) release. Daily pineal 5-HT output is triphasic: (i) 5-HT levels are constant and high during the day; (ii) early in the night, there is a novel sharp rise in 5-HT synthesis and release, which precedes the nocturnal rise in melatonin synthesis; and (iii)

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late in the night, levels are low. To operate surgically on the subjects and use microdialysis, a circular opening was created in the skull by using a dental burr drill equipped with a shank diamond wheel point. The pia matter that covers the surface of the pineal was carefully removed to expose the pineal then the probe is inserted.

**The reference discloses the surgical steps for inserting monitoring probe of microdialysis in the pineal tissue.**

Regarding claim 19, the different time periods recited would not limit the claims since it includes long term, short term, continuous or periodic. Accordingly, any time terms disclosed in the references would read on the instant claim.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include the surgical steps disclosed by Sun to insert the probe into the subject skull to monitor the output of the chemicals secreted by the pineal and the to monitor different biological conditions controlled by the circadian clock. The skilled artisan would expect favorable results in combining the surgical steps to the monitoring method to improve disorders controlled by the circadian rhythm.

The new amendments to the claims which requires the surgical step of "opening the subject's skull dorsal to the subject's confluence of the sinuses".

Ziyal teaches operative technique to expose the pineal to excise pineal tumors wherein craniotomy was performed on one side up to the superior sagittal sinus avoiding injuries to the venous sinuses. The recitation of using a hook is not limiting the claim since various surgical tools can be used for one procedure depending on the objective of the surgery. Note that Ziyal's operative step is to expose the pineal without damaging the tissue which could be successfully achieved by the surgical instrument used by Ziyal.

Further, Lu teaches a method to reach the pineal gland describing that some birds were anaesthetized and a mid-sagittal incision was made in the scalp. Using a dental drill, an approximately 1 cm circular skull cap was removed to expose the dura mater through which the pineal gland could be observed at the confluence of the longitudinal and lateral veins. The dura was carefully cut to expose the pineal gland, which was rapidly removed with mouse-toothed forceps. The dura was replaced, followed by the skull cap, and the scalp was sutured closed. The wound was treated with nitrofurazone powder, and the bird was allowed to recover on a heated pad. The reference teaches that these surgical procedures were known previously with one exception that the pineal gland was not actually removed (see arrow in page 766).

**Thus the two references teach the step of opening the skull over the sinuses to expose the pineal and both disclose that the subject was not sacrificed after the procedure.**

Ziyal and Lu did not teach the step of "pressing the dorsal cerebellum downward" which is the new amendment to claim 17. However, the amendment is a very logical surgical step performed for years in different surgeries wherein the surgeon presses downward an organ anterior to or surrounding said organ (the cerebellum in the instant case) to bulge out a neighboring organ hidden posterior to the pressed organ (for evidence see J. O'leary, Uterine ligation in the control of intractable postpartum hemorrhage, *AJOG* 94 (1966): 920 that teaches pressing the urinary bladder downwards to expose the head of the uterus.)

Thus it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use such manipulation to expose the pineal since the animals should be kept alive for monitoring and minimal damage to the brain tissue. Applicant claims an improved surgical method; however, the claims do not reflect this improvement since Ziyal and Lu recited the same steps.

***Response to Arguments***



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1. Applicant's arguments filed 3/4/2008 have been fully considered but they are not persuasive. Applicant argues that:

**2. Rejection under 35 U.S.C. §112 first paragraph:**

- The specification adequately defines the term "agent." For example, at page 13, [0062], the specification defines the term "agent" to include "pharmacologically active agents, therapeutic agents, biological molecules, amino acids...neuropeptides...mammalian tachykinins...agonists, antagonists and derivatives of all of the above." Also, the specification states that the term "agent" can be used interchangeably with "chemical" and "metabolite".

**To respond:** what Applicant relies upon in the arguments as a definition does not help an artisan to envisage the invention. It is nevertheless without an example of this "agent", a structure, or a mode of action that conveys a sense that Applicant had possession of the claimed invention. What Applicant is considering as a definition is just a categorizing of the hundreds of agents which may be identified to modulate a biological condition. However, it does not describe any information that shows that Applicant had possession of the claimed invention. Again, since there is no structure/function relationship of the agents, which are merely described by what they may do in vivo, the specification does not properly describe such a genus.

- The claims require that the agent modulates a preselected condition controlled by the circadian clock. Thus, the claimed method is not directed to identifying any agent, but an agent that modulate a preselected condition controlled by the circadian clock.

**To respond:** the argument is not clear since claim 1 recites "a method for identifying at least one agent". Further, it is not clear how a person having ordinary skill in the art would be able to identify an agent to modulate a preselected condition wherein the "agent" is not described or exemplified or its mode of action is explained.

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▪ The claimed invention is drawn toward a method of identifying an agent that modulates a preselected condition. The present invention is not directed to a product or a composition. Accordingly, the specification adequately provides written description for the claimed invention. Therefore, it is respectfully requested that this rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

**To respond:** the MPEP explains that the written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. In contrast, without such a correlation, the capability to recognize or understand the structure from the mere recitation of function and minimal structure is highly unlikely. In this latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 (written description requirement not satisfied by merely providing "a result that one might achieve if one made that invention"); *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming a rejection for lack of written description because the specification does "little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). (MPEP, Methodology for Determining Adequacy of Written Description). In the instant case, the act of identifying an agent which modulates a preselected biological condition correlates between the identification of such an agent and its function. If the agent is not sufficiently described, a skilled artisan would not be able to envisage the agent by knowing the function which is "modulating". Thus the written description of the claimed invention is not adequate.

**3. Rejection under 35 U.S.C. §112 second paragraph:**

- Applicant is alleging that the instant amendments to claim 8 can be indirectly defined in the specification and offers a definition in the arguments alleging that the physiological state of a tissue refers to the state of the tissue under normal physiological conditions".

- **To respond:** this definition should be provided through the specification not in the arguments. It is respectfully noted that people having ordinary skill in the art should find the claims definite through the specification. The claim recites, "wherein the preselected biological condition is the physiological state of a tissue", the phrase "physiological state" is not clear since all tissues are in a specific physiological state at all times. The claim is vague.

**4. Rejection under 35 U.S.C. §103:**

- Drijfhout et al. disclose an entirely different method of accessing the pineal, a method whereby tissue surrounding the pineal is inevitably injured and animals are sacrificed the day after surgery.

**To respond:** instant claims were rejected properly over Drijfhout wherein the claims were not limited to specific surgical procedures of how to reach the pineal. Newly amendments claims are further rejected over Ziyal et al. and Lu et al. which renders this argument moot.

- Arendt does not disclose any surgical methods but instead provides a review of using locomotor activity as a marker for measuring melatonin's effects. Arendt does not disclose any surgical methods.

**To respond:** Arndt is relied upon for teaching the treatment of condition or disorders other than sleep disorders which can be a therapeutic agent for some conditions such as psychiatric problems.

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▪ The cited references do not disclose opening the skull at this point. Furthermore, the cited references do not teach lifting the nonpineal tissue with a hook or exposing the pineal gland by pressing down on the dorsal cerebellum.

**To respond:** The claims as amended and new claims are now properly rejected by further relying upon Ziyal and Lu wherein the surgical steps are disclosed.

### ***Conclusion***

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### ***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nabila G Ebrahim/  
Examiner, Art Unit 1618

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